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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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|---|---|---|---|
| **Applicant(s):** | Shaun A. Kirkpatrick, et al. | **Examiner:** | Konstantina Katcheves |
| **Serial No.:** | 09/433,429 | **Art Unit:** | 1636 |
| **Filed:** | November 4, 1999 | **Docket:** | 11160 |
| **For:** | PRODUCTION OF A BIOLOGICAL FACTOR AND CREATION OF AN IMMUNOLOGICALLY PRIVILEGED ENVIRONMENT USING GENETICALLY ALTERED SERTOLI CELLS | | |

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

**DECLARATION OF DR. CRAIG HALBERSTADT UNDER 37 C.F.R. §1.132**

Sir:

I, Craig Halberstadt, declare the following:

1. I am currently employed by the Carolinas Medical Center and hold the position of Director, Tissue Engineering at the Cannon Research Building, Charlotte, North Carolina.

2. I hold a Bachelor of Science (B.S.) Degree in Microbiology and a Doctorate Degree in Bioengineering both from the University of Michigan. I have conducted research in Cell Transplantation since 1991, and have authored 23 publications in the field of Cell Transplantation and Tissue Engineering. In addition, I am an inventor named on eight issued US patents relating to the fields of Cell Transplantation and Tissue Engineering. A true and correct copy of my curriculum vitae is attached hereto as **Exhibit A**.

3. I have reviewed the above-identified application (hereinafter referred to as the '429 application) and I am familiar with the subject matter therein. I have read the Office Action

dated July 29, 2003, issued December 3, issued to the '429 application, and have been asked to comment on issues raised by the Examiner in the Office Action.

4. It is my understanding that the Examiner contends that the specification does not provide any data showing that the biological factor is expressed in the subject, or that the Sertoli cells create immunologically privileged sites *in vivo*. The Examiner is of the opinion that, absent further evidence and in view of the unpredictability of the art, it would take undue experimentation for those skilled in the art to make and use the claimed Sertoli cells.

5. Exhibit B describes experiments that were conducted in my laboratory and a laboratory at the University of Alberta in Edmonton Canada to investigate whether Sertoli cells (SCs) isolated from transgenic mice, which were engineered to produce green fluorescent protein (GFP), would survive allogeneic rejection and continue to express GFP.

6. First, it was confirmed that GFP was expressed in SCs of the TgN(GFPU)5Nagy mice, but not the wild-type (non-transgenic) mice. SC aggregates expressing GFP were then transplanted under the left kidney capsule of immunocompromised SCID mice. GFP positive SCs were detected in 100% of the grafts at both 30 and 60 days post-transplant. See Figures 2-3.

7. To determine whether GFP expressing SCs can survive as allografts and continue to produce the transgene, SC aggregates expressing GFP were transplanted under the left kidney capsule of H-$2^d$ Balb/c mice. GFP positive SCs were detected in grafts from Balb/c mice at both 30 and 60 days post-transplant. See Figures 5-6. In contrast, when islet cells (which are nonimmunoprivileged cells) from TgN(GFPU)5Nagy mice were transplanted to the renal subcapsular space of diabetic Balb/c mice, all animals rejected these islets within 17 days. See Figure 4.

8. It is my scientific opinion that, the results in Exhibit B indicate that SCs can be altered to express foreign proteins and that the genetically altered SCs can survive transplantation in an allogeneic recipient and continue to express the heterologous protein. The

expression of the heterologous protein does not inhibit the ability of SCs to protect themselves against allogeneic rejection in a recipient animal.

9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that those statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

By: _____

Dated: 11/24/03